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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/918,537	08/22/1997	KOICHI AKASHI	LSJU-64PAT	6190

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/918,537	Applicant(s) AKASHI ET AL.	
	Examiner Janice Li	Art Unit 1632	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in Paper No. 13 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 12-18 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Claims 1-11 are under current examination.

Priority

This application was filed August 22, 1997.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because of the claim recitation, "a substantially pure composition". Although the claim defines the characteristics of the

cells in the subsequent phrase (at least 95%...), a composition comprises more than one component, it is unclear which components "substantially" describe and criteria considered being pure, thus, the metes and bounds of the claims are unclear.

Claim 3 is vague and indefinite because of the claim recitation, "blast cells". The specification does not define the term, the meaning of the term is unclear in the context of the claim, and thus the metes and bounds of the claim are unclear. For the purpose of compact prosecution, the Examiner will interpret the term as cells in a proliferative mode in a cell lineage.

Claims 7-11 are vague and indefinite. The claims are directed to a method for enrichment for a composition of mammalian lymphoid progenitor cells comprising a step of, "selecting for those cells", however, it is unclear how the selection is being conducted or means for selection. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, and 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Galy* (US 5,972,627), *Moore et al* (Blood 1995;86:1850-60), in view of *Galy et al* (Immunity 1995;3:459-73).

Claims 1-3 and 6 are drawn to a composition comprising mammalian common lymphoid progenitor cells, wherein at least 95% of the cells bear surface markers for c-kit^{lo}, IL-7Rα^+ and Lin$^-$, and wherein said progenitor cells are capable of giving rise to T, B, and NK cells, wherein the cells are further characterized as Thy-1$^-$, and blast cells; wherein the cells are genetically modified to comprise an exogenous DNA vector. Claims 7-9 are drawn to a method of enrichment for said cell composition, wherein the hematopoietic cells from bone marrow, peripheral blood are used initially for selection.

Galy teaches a population of the mammalian common lymphoid progenitor cells (hematopoietic cells enriched for dendritic and lymphoid cell progenitors, claim 1), which are capable of giving rise to T, B, and NK cells, bearing Lin$^-$, Thy-1$^-$, and CD45$^+$ markers (fig. 1, middle and right panel), and further bear low levels (clearly positive to negative) of *C-kit* marker (column 16, lines 33-42). Because the cells are in the lymphoblastoid gate, they are considered as blast cells. Claims 1 and 5 of cited patent further describe that cells bearing the recited markers are greater than 95% in the obtained cell population. *Galy* also teaches that said cells could be genetically modified (column 5, lines 27-30, and column 12). *Galy* goes on to teach a method for purifying and enriching said cells from hematopoietic cell source such as bone marrow and peripheral blood using antibodies recognizing cell surface markers (paragraph bridging columns 8-9).

"SELECTION OF THESE PROGENITOR CELLS NEED NOT BE ACHIEVED WITH A MARKER SPECIFIC FOR THE CELLS. BY USING A COMBINATION OF NEGATIVE SELECTION AND POSITIVE SELECTION, ENRICHED CELL POPULATIONS CAN BE ACHIEVED" using various separation methods such as magnetic separation, affinity chromatograph and flow cytometry (column 9). One of the methods is measuring the cells by size, granularity, and propidium iodide exclusion in the live cell gate using FACS (column 20, lines 59-65). *Galy* teach using many different cell surface markers, such as those listed in tables 1, 2 and 7, but does not teach using IL-7 receptor alpha.

Moore et al teach that IL-7 or IL-Ra is closely associated with early T-cell proliferation and expansion, but not in differentiation (meaning they are committed lymphoid progenitor cells). *In vivo* administration of anti-IL-7R antibody resulted in a marked decrease in thymic cellularity (blocking the binding of IL-7 with IL-7R), proving the presence of IL-7 receptor on the surface of thymic progenitor cells (right column page 1850). They also teach that this subset of intrathymic progenitor cells contain T, B, NK, and dendritic cells, but not myeloid lineage cells (left column page 1850).

Galy et al teach that human T, B, NK, and dendritic cells arise from a common bone marrow progenitor cell subset, characterized by CD34+, Lin-, CD10+, and CD45RA+ surface markers (Summary).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Galy,* by simply including IL-7R as one of the markers for enrichment of lymphoid progenitor cells with a reasonable expectation of success. The ordinary skilled artisan would have been

motivated to modify the method because it provides additional criteria for purification (a positive selection process as taught by *Galy*), thus, achieving better enrichment of lymphoid progenitor cells. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-4, and 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Galy* (US 5,972,627), *Moore et al* (Blood 1995;86:1850-60), and *Galy et al* (Immunity 1995;3:459-73) as applied to claims 1-3 and 6-10 above, further in view of *Kawamoto et al* (Int Immunol 1997 July;9:1011-1019).

Claims 4 and 11 are drawn to selecting the desired cells by Sca-1^{lo} marker. The combined teachings of *Galy*, *Moore et al*, and *Galy et al* fails to teach the particular marker. However, before the effective filing date of the instant application, *Kawamoto et al* teach the Sca-I marker and its association with lineage commitment of hematopoietic stem cells. They teach that Sca-1^{+} population are multipotent or unipotent progenitor cells giving rise to both lymphoid and myeloid cells, whereas Sca-1^{-} population only give rise to one of the T, B, or M cells (abstract). They go on to teach, "COMMITMENT TO THE M LINEAGE BEGINS AT THE SCA-1+ STAGE, WHEREAS COMMITMENT TO THE B LINEAGE OCCURS AFTER LOSING THE SCA-1 ANTIGEN".

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Galy, Moore et al*, and *Galy et al* by simply including Sca-1 as one of the markers for the enrichment of lymphoid progenitor cells, with a reasonable expectation of success. The ordinary

skilled artisan would have been motivated to modify the method because Sca-1^{lo} could eliminate some of the myeloid progenitor cells (a negative selection process as taught by *Galy*) while permit the lymphoid progenitors remain in the population, thus, achieving better enrichment of lymphoid progenitor cells. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-3, 5, and 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Galy* (US 5,972,627), *Moore et al* (Blood 1995;86:1850-60), and *Galy et al* (Immunity 1995;3:459-73) as applied to claims 1-3 and 6-10 above, further in view of *Kincade et al* (Int Immunol 1997 July;9:1011-1019) and *Ballas et al* (J Immunol 1990;145:1039-45).

Claim 5 is drawn to additional markers, $CD43^{lo}$, HSA^{lo}, $CD45^{+}$, and Mel-14^{-}. The combined teachings of *Galy*, *Moore et al*, and *Galy et al* teach $CD45^{+}$, but fails to teach $CD43^{lo}$, HSA^{lo}, and Mel-14^{-}. However, before the effective filing date of the instant application, *Kincade et al* teach selective regulation of B lymphocyte precursor (lymphoid progenitor) cells by targeting CD45RA, CD43, IL-7, and heat stable antigen (HSA, column 10, lines 3-9). *Ballas et al* teach that thymocytes are MEL-14^{-}, whereas mature peripheral NK cells are MEL-14^{+}.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Galy, Moore et al*, and *Galy et al* by simply including $CD43^{lo}$, HSA^{lo}, and Mel-14^{-} as markers for the enrichment of lymphoid progenitor cells, with a reasonable expectation of success. The ordinary

skilled artisan would have been motivated to do so because additional markers serve to verifying whether the selected cell population is enriched of lymphoid progenitor cells or contaminated with mature lymphocytes. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
September 3, 2002

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER